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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/501,102	02/09/2000	Man Sung Co	WYS-00401	3404

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EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	

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10/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/501,102	CO ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *145,147 and 149-154* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *145, 147 and 149-154* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action as been withdrawn pursuant to 37 CFR 1.114.

Applicant's submission, filed on 09/25/2007, has been entered.

Applicant's amendment, filed on 09/25/2007, has been entered.

Claims 143-144, 146, 148 and 155-160 have been canceled.
Claims 1-142 have been canceled previously.

Claims 145, 147, 149 and 154 have been amended.

Claims 145, 147 and 149-154 are pending.

Claims 145, 147 and 149-154, as they read on the elected invention, including the elected species of the combination of anti-B7-1 antibodies, anti-B7-2 antibodies and cyclosporin or rapamycin in the claimed methods are under consideration in the instant application.

Therefor, the newly amended recitation of administering a third agent, is read on administering cyclosporin or rapamycin as the third agent only.

The newly submitted third agents other than cyclosporin or rapamycin (as the elected species; see Response to Restriction Requirement, filed 12/27/2005 and the Office Action, mailed 04/10/2006) are directed to or encompass third agents that differ in structure and modes of action as well as expression to such an extent and require non-coextensive searches to such an extent that they are considered patentable distinct. Further, these members of the prostate antigens do not share a substantial structural feature essential to a common utility do not have common structure to a common utility.
Therefore, they are patentably distinct.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits.

Accordingly, the third agents other than cyclosporine or rapamycin are withdrawn from consideration as being directed to a non-elected invention. See 37 C.F.R. 2(b) and M.P.E.P. 821.03.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Office Action.

This Action will be in response to applicant's arguments, filed 09/25/2007.

The rejections of record can be found in the previous Office Actions, mailed 04/10/2006, 11/06/2006 and 05/07/2007 and 06/25/2007

3. Priority.

Applicant's arguments, filed 09/25/2007, and the examiner's position on the priority of the instant claims are essentially the same of record.

Currently, applicant's arguments rely upon the following.

Applicants traverse the foregoing and respectfully point out that that USSN 09/249,011 (US Patent No. 6,972,125) contains numerous teachings of the utilization of B7-1 and B7-2 antibodies without inhibitors of CD40 or CD40 ligand. In particular, Applicants direct the Examiner to Examples 8-11 and Figures 8-9, all of which demonstrate the use of B7-1 and B7-2 antibodies without inhibitors of CD40 or CD40 ligand. Applicants respectfully remind the Examiner that a lack of literal basis in the specification for a negative limitation may not be sufficient to establish a *prima facie* case for lack of descriptive support. *Ex parte Parks'*, 30 USPQ2d 1234, 1236 (Bd. Pat. App. & Inter. 1993), MPEP 213.05(i).

Further, in contrast to the Examiner's contention, support for the use of B7-1 and B7-2 antibodies without inhibitors of CD40 or CD40 ligand may also be found in the instant specification, in Examples 16-23, and Figures 18-23 and 26-28. Reconsideration and withdrawal of this rejection, as it applies to claim 145, is respectfully requested.

Applicants traverse and respectfully point out that molecules inhibiting the CD40/CD40 ligand costimulatory interaction were well-known in the art at the time of filing. For example, de Boer et al. (US Patent No. 5,677,165; issued October 14, 1997) and Armitage et al. (US Patent No. 5,961,974; issued October 5, 1999) each demonstrate that antibody-based inhibition of the CD40/CD40 ligand interaction was generally known at the time the instant application was filed. In addition, inhibition of the CD40/CD40 ligand interaction via other methods, such as the use of soluble CD40 fusion proteins (Gray et al., J Exp Med, 1994, 180: 141), were well known in the art at the time of filing. Applicants have amended claims 145 and 154 to recite lack of inhibition of the "costimulatory interaction" between CD40/CD40 ligand.

In light of these amendments and the aforementioned disclosures in the art at the time of filing, Applicants respectfully request reconsideration and withdrawal of this rejection.

Here, again, applicant's arguments have been fully considered but have not been found convincing essentially for the reasons of record.

As addressed previously and reiterated herein for applicant's convenience,
It appears that applicant is relying upon limited species (e.g., "α CD40 ligands" though it is not clear what "α CD40 ligands" was intended to mean, since this does not appear to be a designation of art; "anti-CD40 ligands" with anti-CD40 antibodies as the the only designation of a possible inhibitor of CD40:CD40 ligand interactions clearly named in the priority documents).

Also, it was known at the time the invention was made, particularly as the time of the priority documents, that anti-CD40 antibodies were agonistic as well.

Also, with CD40L, monomeric CD40L is considered antagonistic, while multimeric CD40L is considered an agonistic.

While the Examples of the priority documents and herein do not necessarily employ inhibitors of CD40 or CD40 ligand interactions",
Clearly, the priority documents and the instant disclosure as well contemplate combination therapy (e.g. see the instant Summary of the Invention).

Further, it appears that applicant's arguments rely, in part, on disclosures not necessarily found in the instant specification, or the priority documents.

Applicant's arguments have not been found persuasive for the reasons of record and again, reiterated herein for applicant's convenience.

The effective filing date of the instant claims is deemed as follows.

While It appears that priority USSN 09/249,011, now U.S Patent No. 6,972,125 provides for the recitation of "α CD40 ligands" as another drug that can be administered with B7-1- / B7-2-specific antibodies" (e.g., see column 18, paragraph 2 of U.S. Patent No. 6,972,125),
again, this priority document does not provide sufficient written description of the newly amended claim limitation "wherein an inhibitor of CD40 or CD40 ligand costimulatory interaction is not administered to the transplant recipient", as broadly claimed in the instant claims.

While It appears that priority USSN 09/339,596, now U.S Patent No. 6,913,747 provides for the recitation of "anti-CD40 ligands" as another drug that can be administered with B7-1- / B7-2-specific antibodies" (e.g., see column 24, paragraph 5 of U.S. Patent No. 6,913,747);
again, this priority document does not provide sufficient written description of the newly amended claim limitation "wherein an inhibitor of CD40 or CD40 ligand costimulatory interaction is not administered to the transplant recipient", as broadly claimed in the instant claims.

While it appears that the instant USSN 09/501,102 provides for the recitation of "anti-CD40 pathway inhibitors (e.g. anti-CD40 antibodies, anti-CD40 ligand antibodies and small molecule inhibitors of the CD40 pathway" as another drug that can be administered with B7-1- / B7-2-specific antibodies" (e.g., see page 42, paragraph 2 of the instant specification);

again, the instant application does not provide sufficient written description of the newly amended claim limitation "wherein an inhibitor of CD40 or CD40 ligand costimulatory interaction is not administered to the transplant recipient", as broadly claimed in the instant claims.

Again, the instant claims now recite limitations which were not clearly disclosed in the priority applications as well as the specification as-filed, and would have changed the scope of the priority applications and do change the scope of the instant disclosure as-filed.

Further, neither the priority applications nor the instant application have provides a sufficient description of a representative number of species of "inhibitors of CD40 or CD40 ligand" to represent the entire genus of "inhibitors of CD40 or CD40 ligand", broadly encompassed by the current claims.

As noted above, it is not clear what "α CD40 ligands" was intended to mean, since this does not appear to be a designation of art.

Also, it appears that anti-CD40 antibodies were the only clear designation of a possible inhibitor of CD40:CD40 ligand interactions in the priority documents

Further, there was no discussion of agonistic and antagonistic properties of anti-CD40 antibodies nor of the CD40 ligand itself either in the priority documents or in the instant application as filed.

For example, it cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679, 683 (CCPA 1972). Also see MPEP 2163.05.

Therefore, reliance upon the genus of "drugs" and the disclosure of certain "inhibitors of CD40 or CD40 ligand" (e.g. anti-CD40 antibodies, anti-CD40 ligand antibodies) does not provide sufficient written description for certain "inhibitors of CD40 or CD40 ligand", as currently claimed.

As indicated previously, there does not appear to be sufficient description showing *possession of the necessary functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics*, sufficient to show the applicant was in possession of the genera of "α CD40 ligands" "anti-CD40 ligands" and "small molecule inhibitors of the CD40 pathway" consistent with written description provisions of 35 USC 112, first paragraph, and the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, § 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday January 2001.

Therefore, there appears to be insufficient written description for the phrase "wherein an inhibitor of CD40 or CD40 ligand costimulatory interaction is not administered to the transplant recipient", as broadly claimed in the instant claims in the priority documents as well as in the instant specification.

Therefore, given the lack of written description of the claimed methods as indicated herein and below, the instant claims do not appear to have the priority date of USSNs 09/339,596 and 09/249,011.

In addition with respect to applicant's newly amended claims, filed 09/25/2007, it is noted that the recitation of the newly submitted Markush of
"third agents selected from the group consisting of: calcineurin inhibitor, steroid, and immunosuppressive agent that arrest the growth of immune cells, methotrexate, transplant salvage pathway inhibitor, IL-2 receptor antagonist, and analogs thereof, and wherein an inhibitor of the CD40/ CD40 ligand costimulatory interaction is not administered to the transplant recipient"
are not readily apparent in applicant's priority documents, 09/339,596 and 09/249,011, particularly the written description of
"calcineurin inhibitor", "immunosuppressive agent that arrest the growth of immune cells", "transplant salvage pathway inhibitor", "IL-2 receptor antagonist" and "analogs" in addition to "an inhibitor of the CD40/ CD40 ligand costimulatory interaction".

If applicant desires priority back to their priority documents,
applicant is invited to point out and provide documentary support for the priority of the instant claims

Applicant is reminded that such priority for the instant limitations requires written description and enablement under 35 U.S.C. § 112, first paragraph.

A claim as a whole has only one effective filing date.
See Studiengelsellschaft Kahle m.b.H. v. Shell Oil Co. 42 USPQ2d 1674, 1677 (Fed. Cir 1997).

4. Claims 145-147 and 149-154 stand rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed.

The specification as originally filed does not provide support for the invention as now claimed:

"wherein an inhibitor of CD40 or CD40 ligand costimulatory interaction is not administered to the transplant recipient".

Applicant's previous amendments simply asserted that no new matter has been added and does not provide any direction to the written support of the newly added claim either in the instant application or in the priority applications.

Applicant's arguments, filed 09/25/2007, and the examiner's rebuttal are essentially the same of record and addressed above in Section 3.

Applicants also respectfully point out that the instant specification contains numerous examples of the administration of B7-1 and B7-2 antibodies in the absence of an inhibitor of the costimulatory interaction between CD40 and CD40 ligand. Applicants direct the Examiner to Examples 16-23, and Figures 16-23 and 26-28 of the instant specification, all of which demonstrate the use of B7-1 and B7-2 antibodies without inhibitors of the costimulatory interaction between CD40 and CD40 ligand. In particular, Applicants point out that Example 22 of the instant specification discloses the use of B7-1 and B7-2 antibodies alone and in combination with several other immunosuppressive agents, such as cyclosporin A, rapamycin, and steroids, but not inhibitors of costimulatory interactions between CD40 and CD40 ligand. Applicant respectfully remind the Examiner that a lack of literal basis in the specification for a negative limitation may not be sufficient to establish a *prima facie* case for lack of descriptive support. *Ex parte Parks'*, 30 USPQ2d 1234, 1236 (Bd. Pat. App. & Inter. 1993), MPEP 213.05(i).

Furthermore, as stated above, molecules inhibiting the CD40 - CD40 ligand costimulatory interaction were well-known in the art at the time of filing (see de Boer et al., US Patent No. 5,677,165, issued October 14, 1997; Armitage et al., US Patent No. 5,961,974, issued October 5,1999; Gray et al., J Exp Med, 1994, 180: 141).

In light of the amendment of claims 145 and 154, the written description available in the instant specification, and the aforementioned disclosures of methods of inhibiting CD40 - CD40 ligand interactions available in the art at the time of filing, Applicants respectfully request reconsideration and withdrawal of these rejections.

For the reasons of record, the recitation of "wherein an inhibitor of CD40 or CD40 ligand costimulatory interaction is not administered to the transplant recipient" is not readily apparent either in the pending or in the earlier priority applications.

While It appears that priority USSN 09/249,011, now U.S Patent No. 6,972,125 provides for the recitation of "α CD40 ligands" as another drug that can be administered with B7-1- / B7-2-specific antibodies" (e.g., see column 18, paragraph 2 of U.S. Patent No. 6,972,125),

this priority document does not provide sufficient written description of the newly amended claim limitation "wherein an inhibitor of CD40 or CD40 ligand costimulatory interaction is not administered to the transplant recipient", as broadly claimed in the instant claims.

While It appears that priority USSN 09/339,596, now U.S Patent No. 6,913,747 provides for the recitation of "anti-CD40 ligands" as another drug that can be administered with B7-1- / B7-2-specific antibodies" (e.g., see column 24, paragraph 5 of U.S. Patent No. 6,913,747);

this priority document does not provide sufficient written description of the newly amended claim limitation "wherein an inhibitor of CD40 or CD40 ligand costimulatory interaction is not administered to the transplant recipient", as broadly claimed in the instant claims.

While It appears that the instant USSN 09/501,102 provides for the recitation of "anti-CD40 pathway inhibitors (e.g. anti-CD40 antibodies, anti-CD40 ligand antibodies and small molecule inhibitors of the CD40 pathway" as another drug that can be administered with B7-1- / B7-2-specific antibodies" (e.g., see page 42, paragraph 2 of the instant specification);

the instant application does not provide sufficient written description of the newly amended claim limitation "wherein an inhibitor of CD40 or CD40 ligand costimulatory interaction is not administered to the transplant recipient", as broadly claimed in the instant claims.

The instant claims now recite limitations which were not clearly disclosed in the priority applications as well as the specification as-filed, and would have changed the scope of the priority applications and do change the scope of the instant disclosure as-filed.

Further, neither the priority applications nor the instant application have provides a sufficient description of a representative number of species of "inhibitors of CD40 or CD40 ligand costimulatory interaction" to represent the entire genus of "inhibitors of CD40 or CD40 ligand costimulatory interaction", broadly encompassed by the current claims.

Further, neither the priority applications nor the instant application have provides a sufficient description of a representative number of species of "inhibitors of CD40 or CD40 ligand costimulatory interaction" to represent the entire genus of "inhibitors of CD40 or CD40 ligand", broadly encompassed by the current claims.

As noted above in Section 3, it is not clear what "α CD40 ligands" was intended to mean, since this does not appear to be a designation of art.
Also, it appears that anti-CD40 antibodies were the only clear designation of a possible inhibitor of CD40:CD40 ligand interactions in the priority documents
Further, there was no discussion of agonistic and antagonistic properties of anti-CD40 antibodies nor of the CD40 ligand itself either in the priority documents or in the instant application as filed.

While the Examples of the priority documents and herein do not necessarily employ inhibitors of CD40 or CD40 ligand interactions",
Clearly, the priority documents and the instant disclosure as well contemplate combination therapy (e.g. see the instant Summary of the Invention).

Further, it appears that applicant's arguments rely, in part, on disclosures not necessarily found in the instant specification, or the priority documents.

Applicant's arguments have not been found persuasive for the reasons of record and again, reiterated herein for applicant's convenience.
For example, it cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679, 683 (CCPA 1972). Also see MPEP 2163.05.

Therefore, reliance upon the genus of "drugs" and the disclosure of certain "inhibitors of CD40 or CD40 ligand" (e.g. anti-CD40 antibodies, anti-CD40 ligand antibodies) does not provide sufficient written description for certain "inhibitors of CD40 or CD40 ligand", as currently claimed.

Further, there does not appear to be sufficient description showing possession of *the necessary functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genera* of "α CD40 ligands" "anti-CD40 ligands" and "small molecule inhibitors of the CD40 pathway" consistent with written description provisions of 35 USC 112, first paragraph, and the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, § 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday January 2001.

Given the lack of sufficient description showing possession of the necessary functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genera of "α CD40 ligands" "anti-CD40 ligands" and "small molecule inhibitors of the CD40 pathway",
applicant's newly added limitation of reciting a negative limitation based upon the limited disclosure in the instant and priority applications raised new matter under 35 USC 112, first paragraph, written description.

Therefore, there appears to be insufficient written description for the phrase "wherein an inhibitor of CD40 or CD40 ligand costimulatory interaction is not administered to the transplant recipient", as broadly claimed in the instant claims in the priority documents as well as in the instant specification.

The specification as filed does not provide a sufficient written description or set forth the metes and bounds of this phrase. The specification does not provide blaze marks nor direction for the instant methods encompassing the above-mentioned "limitation", as currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office Action.

Alternatively, applicant is invited to provide sufficient written support for the "limitation" indicated above.
See MPEP 714.02 and 2163.06

Applicant's arguments of record and the examiner's rebuttal are essentially the same of record and addressed herein and above in Section 3.

Applicant's arguments have not been found persuasive.

5. Claims 145, 147 and 154 stand rejected under 35 U.S.C § 102(e) as being anticipated by Freeman et al. (U.S. Patent No. 6,605,279) (see entire document) essentially for the reasons of record.

Applicant's arguments, filed 09/25/07, have been fully considered but have not been found convincing essentially for the reasons of record.

Applicant simply relies upon the assertion that Freeman et al. does not teach each an every element of the instant claims and the assertion that amending claims 145 and 147 renders the foregoing rejection moot.

However, applicant has not pointed out the deficiencies in the rejection of record.

Further, applicant is reminded that the instant claims are read on the elected invention, including the elected species of the combination of anti-B7-1 antibodies, anti-B7-2 antibodies and cyclosporin or rapamycin in the claimed methods are under consideration in the instant application.

Therefore, the newly amended recitation of administering a third agent, is read on administering cyclosporin or rapamycin as the third agent only.

Applicant's arguments have not been found persuasive.

The following is reiterated for applicant's convenience.

Freeman et al. teach methods of downregulating or suppressing T cell mediated immune responses, including the use of B7-1-specific and B7-2-specific antibodies in conjunction with other immunomodulating reagents such as cyclosporine or FK506, including it usefulness in situations of tissue and organ transplantation as well as GVHD (see entire document, particularly Other Therapeutic Reagents on columns 32-34).

It does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure

Applicant's arguments of record and the examiner's rebuttal are essentially the same of record.

Given the absence of additional rebuttal to the outstanding rejections of record in applicant's request for continued examination under 37 CFR 1.114,
the rejections are maintained for the reasons of record.

6. Claims 145, 147 and 149-154 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Freeman et al. (U.S. Patent No. 6,605,279) in view of the well known use of immunosuppressives such as cyclosporin, FK506 and rapamycin and effective therapeutic antibody dosages in transplantation therapeutic regimens at the time the invention was made, as taught by de Boer et al. (U.S. Patent No. 5,757,034) (1449) essentially for the reasons of record.

Applicant's arguments, filed 09/25/07, have been fully considered but have not been found convincing essentially for the reasons of record.

Applicant simply relies upon the assertions that Freeman et al. fails to teach or suggest the claims invention and the assertion that amending claims 145 and 147 renders the foregoing rejection moot.

However, applicant has not pointed out the deficiencies in the rejection of record.

Further, applicant is reminded that the instant claims are read on the elected invention, including the elected species of the combination of anti-B7-1 antibodies, anti-B7-2 antibodies and cyclosporin or rapamycin in the claimed methods are under consideration in the instant application.

Therefore, the newly amended recitation of administering a third agent, is read on administering cyclosporin or rapamycin as the third agent only.

Applicant's arguments have not been found persuasive.

The following is reiterated for applicant's convenience.

Freeman et al. teach methods of downregulating or suppressing T cell mediated immune responses, including the use of B7-1-specific and B7-2-specific antibodies in conjunction with other immunomodulating reagents such as cyclosporine or FK506, including it usefulness in situations of tissue and organ transplantation as well as GVHD (see entire document, particularly Other Therapeutic Reagents on columns 32-34).

While Freeman et al. teach the administration of therapeutically effective amounts of the therapeutic compositions, wherein amounts of effective dosages are administered for periods of time necessary to achieve the desired results (e.g. see Administration of Therapeutic Forms of B Lymphocytes Antigens on columns 37-39), Freeman et al. differs from the claimed methods by not disclosing the well known use of immunosuppressives such as rapamycin and effective therapeutic antibody dosages in transplantation therapeutic regimens at the time the invention was made .

De Boer et al. teach the use of B7-specific antibodies in combination with immunosuppressive agents such as cyclosporin, FK506 and rapamycin (e.g., see column 14, paragraphs 2-3) in therapeutic amounts and modes of administration encompassed by the claimed invention (e.g., see column 16, paragraph 5) (see entire document).

One of ordinary skill in the art at the time the invention was made would have been motivated to modify the teachings of Freeman et al. to incorporate the well known use of immunosuppressives such as as cyclosporin, FK506 and rapamycin and effective therapeutic antibody dosages in transplantation therapeutic regimens at the time the invention was made to achieve the desired therapeutic result of inhibiting graft rejection and promoting long term graft survival with effective amounts of standard immunosuppressives and effective amounts of therapeutic antibodies. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Also, as to the use of a combination of immunosuppressive therapy in transplantations therapeutic regimens,
methods of administration are a result effective variable.

It is well settled that "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." In re Boesch, 617 F.2d 272, 276, 205 USPQ 215, 219 (CCPA 1980). See also Merck & Co. v. Biocraft Labs. Inc., 874 F.2d 804, 809, 10 USPQ2d 1843, 1847-48 (Fed. Cir. 1989) (determination of suitable dosage amounts in diuretic compositions considered a matter of routine experimentation and therefore obvious).

"The test of obviousness is not express suggestion of the claimed invention in any or all of the references but rather what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them." See In re Rosselet, 146 USPQ 183, 186 (CCPA 1965).

"There is no requirement (under 35 USC 103(a)) that the prior art contain an express suggestion to combine known elements to achieve the claimed invention. Rather, the suggestion to combine may come from the prior art, as filtered through the knowledge of one skilled in the art." Motorola, Inc. v. Interdigital Tech. Corp., 43 USPQ2d 1481, 1489 (Fed. Cir. 1997).

An obviousness determination is not the result of a rigid formula disassociated from the consideration of the facts of a case. Indeed, the common sense of those skilled in the art demonstrates why some combinations would have been obvious where others would not. See KSR Int'l Co. v. Teleflex Inc., 82 USPQ2d 1385 (U.S. 2007) ("The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.").

7. No claim allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phillip Gambel, Ph.D., J.D.
Primary Examiner
Technology Center 1600
October 1, 2007